UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,467	11/28/2003	Philippe Du Mesnil	P63187US2	7970

136 7590 01/20/2006

JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER	
WILLIAMS, LEONARD M	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 01/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,467	DU MESNIL ET AL.	
	Examiner	Art Unit	
	Leonard M. Williams	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/192184.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Foreign Priority

The examiner acknowledges the claim to foreign priority under 35 USC 119(a) to FR 98 12 388 (filed October 2, 1998) noted in the oath/declaration filed 11/28/2003.

Status of Claims

The amendment/remarks received 10/19/2005, amending claims 12-20 and canceling claims 1-11 has been entered. Claims 12-20 (amended) are currently pending.

The amendment of claims 13-20 changing the dependency of said claims to claim 12 and not to claim 28 (as originally claimed) is sufficient to overcome the 112-2 rejection over claims 12-20.

Claim 12 was amended only by the deletion of the phrase "...to a human or...". No other amendments were made to claim 12.

The 112-2 rejection of claim 12 for being indefinite is maintained, for reasons set forth below in the response to arguments.

The 102(b) and 103 (a) rejections of claims 12-20 are maintained, for reasons set forth below in the response to arguments.

Response to Arguments

Applicant's arguments filed 10/19/2005 have been fully considered but they are not persuasive. The applicant's make a series of statements on page 8 of the arguments. Some the statements follow:

"Merely that it requires some thought to understand the meaning of a claim term does not render the term indefinite...*S3 Inc. v. nVIDIA*....".

"...The examiner's definition of a claim limitation cannot conflict with the definition given in the specification, which must be used in construing the claims for purposes of examination. *In re Zletz*..."

"...Moreover, perhaps more importantly, the definition of a claim limitation given by the examiner cannot be different than would be given by one of ordinary skill in the art. *In re Cortright*..."

On page 9, the applicant's state:

"The statement of rejection correctly observes that osteoarthrosis is synonymous with osteoarthritis..."

Further the applicant's argue that osteoarthritis and arthritis are different and that osteoarthritis is a non-inflammatory bone-joint disorder and that arthritis is an inflammatory bone-joint disorder. The applicant's then present definitions from the *On Line Medical Dictionary* of arthritis and osteoarthritis in support of these assertions.

The applicant's set forth that from these definitions and assertions that one of ordinary skill in the art would know that osteoarthritis and arthritis are not synonymous and thus there is no indefiniteness to the claim.

The examiner respectfully disagrees. Without wishing to enjoin in a battle of dictionaries the examiner feels it necessary to set forth the thought processes involved in the upholding of the 112-2 rejection of claim 12. First the applicant's do not offer or particularly define the terms osteoarthritis and arthritis in the specification. Second, Stedman's Medical Dictionary 27th edition defines arthritis as "inflammation of a joint or a state characterized by inflammation of joints", further on the definition defines arthritis-degenerative as osteoarthritis. Third, Stedman's Medical Dictionary 27th edition defines osteoarthritis as "arthritis characterized by erosion of articular cartilage, either primary or secondary to trauma or other conditions...". Fourth, Stedman's Medical Dictionary 27th edition defines inflammation as "a fundamental pathologic process consisting of a dynamic complex of cytologic and chemical reactions that occur in the affected blood vessels and adjacent tissues in response to an injury or abnormal stimulization caused by a physical, chemical, or biologic agent....The so-called "cardinal signs" of *i.* are: *rubor*, redness; *calor*, heat (or warmth); *tumor*, swelling; and *dolor*, pain; a fifth sign *functio laesa*, inhibited or lost function, is sometimes added. All of the signs may be observed in certain instances, but no one of them is necessarily always present."

The examiner wishes to particularly point out that the definition of osteoarthritis clearly indicates that it is an "arthritis". Based upon these definitions and the lack of guidance in the specification the examiner determined claim 12 to be indefinite as it claims a process for treating lameness that appears during osteoarthritis by administration of a bisphosphonic acid derivative to a human or animal not suffering from arthritis. As it is clearly known that osteoarthritis is an "arthritis" a patient suffering

from osteoarthritis would *by definition* be suffering from "arthritis", thus the claim is not clear as to what is being claimed (indefinite). The examiner further points out that if the applicant's argue that there is support in the specification that arthritis is defined, the definition could be construed as being repugnant to one of ordinary skill in the art if it teaches that osteoarthritis is not an arthritis.

The rejections of claims 12-20 under 102(b) and 103(a) are maintained for the reasons stated above and for reasons of record as set forth in the previous office action. The crux of the applicant's arguments against the 102(b) rejection over claims 12, 15, 17-18 and 20 consists of the supposed failure of the prior art to teach the claim 12 limitation of "not suffering from arthritis". The examiner points out to the applicant that osteoarthritis is a recognized arthritis and thus the prior art clearly anticipates the treatment of osteoarthritis as it teaches the treatment of arthritis. The failure of the applicant's to clearly claim their invention as pointed out above does not rectify the fact that the prior art teaches the claimed compounds for the treatment of arthritis and for the treatment of conditions due to inflammatory phenomena.

The applicant's also assert that the examiners inherency argument for the treatment of lameness is incorrect. The examiner respectfully disagrees. The examiner again points out that the prior art teaches the treatment of inflammatory conditions and arthritis and that arthritis can lead to lameness and that in the definition of inflammation one of the cardinal signs includes lost function which would include lameness.

For the reasons listed above and for the reasons of record in the last office action the 112-2 rejection of claim 12, the 102(b) rejection of claims 12, 15, 17-18 and 20 and the 103(a) rejection of claims 13-14, 16 and 19 are maintained and reproduced below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 12 is drawn to a "...process for treating lameness that appears during osteoarthrosis comprising administration, to a human or to a human or to an animal not suffering from arthritis..." if the process for treating lameness that appears in conjunction with osteoarthrosis (which is synonymous with osteoarthritis) then the patient by definition must be suffering from arthritis. The examiner is treating claim 12 as a process for treating lameness that appears during osteoarthrosis and not giving weight to the "...not suffering from arthritis...". Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12, 15, 17-18, and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Breliere et al. (US Patent No. 4876248) and as evidenced by applicant's own admission.

Breliere et al. teach, in column 1 lines 5-15, derivatives of methylene-diphosphonic acid represented by formula (I), for use in the treatment of inflammation. Breliere et al. teach, in example 9, the synthesis of Di-(tertiary butylamine) salt of (4-chlorophenyl)thiomethylene-diphosphonic acid (SR 41319) a salt of tiludronic acid (one of the currently exemplified and claimed compounds). Breliere et al. teach, in col. 22-IN VIVO Study, a rat animal model for rheumatoid arthritis wherein the animals were treated with 10mg/kg per day for 6 days to determine the efficacy of the compounds in the treatment of arthritis. In col. 23 lines 10-20, Breliere et al. indicate that the compounds exhibit low toxicity and can be used for the treatment of conditions due to inflammatory phenomena and in particular for the treatment of arthritic conditions anticipating the "...process for treating lameness that appears during osteoarthrosis comprising the administration....of an effective amount of a bisphosphonic acid derivative selected from..." of claim 12, the "...process...comprising administration of 0.001 mg/kg to 100 mg/kg of body weight..." of claim 15, the "...process...comprising the oral administration of the bisphosphonic acid derivative" of claim 17, the "...process...comprising parenteral administration of the bisphosphonic acid derivative" of claim 18, and the "...process...in which the bisphosphonic acid derivative is 4-chlorophenylthiomethylenebisphosphonic acid" of claim 20.

The applicant's state on page 6 lines 5-30, "It has also been possible to demonstrate the anti-inflammatory activity of certain bisphosphonic acid derivatives in a model of arthritis in rats, induced by injection of mycobacterium. However, the authors are unaware of any studies demonstrating the anti-inflammatory activity of these bisphosphonic acid derivatives in pathologies other than arthritis or more generally in other species (and for example in man). More recently, the value of certain bisphosphonic acid derivatives in improving the repair of fractures has been described. Reference will be made in particular to EP 600,834 or U.S. Pat. No. 5,488,041.

In another field, the use of bisphosphonic acid derivatives is also described in the diagnosis of certain bone complaints by scintigraphy. An example of such a use is reported by Keegan K. G., Wilson D. A., Lattimer C. L., Twardock A. R., Ellersieck M. R. (Am. J. Vet. Res., 1996, 57, 415-421) in the scintigraphic evaluation of .sup.99m Tc-methylene diphosphonate labeling of the navicular region in horses with lameness localized on the foot. However no mention is made of the clinical benefit provided by binding the bisphosphonic acid derivative in the bones of the palmar region."

By applicant's own admission bisphosphonates have been used in the treatment of arthritis, have been used for treatment of other bone disorders in humans, and have been used in the diagnosis of lameness in the navicular region of horses.

As a portion of the patient population treated for arthritis would have some degree of lameness and as the compounds disclosed by Breliere et al. are identical to the compounds in the currently claimed method of treating lameness that appear during

osteoarthrosis the lameness is inherently treated by the compounds of Breliere et al. in the general treatment of inflammation and in particular arthritis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-14, 16, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breliere et al. as applied to claims 12, 15, 17-18, and 20 above, and further in view of Barbier et al. (US Patent No. 5488041).

Breliere et al. is as set forth above.

Breliere et al. does not specifically teach the treatment of horses nor the intravenous administration of from 0.1-1 mg/kg/week of tiludronic acid to horses.

Barbier et al. teach, in the abstract and in col. 3 lines 10-35, method of promoting bone repair in human or veterinary medicine which comprises the administration of a

therapeutically effective amount of bisphosphonic acid derivatives (see Formula I). Said method is particularly suitable following a fracture or bone surgery. It includes the use of drugs containing at least one bisphosphonic acid derivative.

Such drugs can be used in human medicine and in veterinary medicine.

Such drugs can be administered by different modes of administration, for example orally, parenterally, transdermally or by means of an implant.

When a drug for oral administration is prepared, it is possible to use any suitable excipient and in particular an excipient which facilitates the absorption of the drug, such as sodium laurylsulfate.

The administration doses of the drug according to the invention depend on the bisphosphonic acid derivative used, the mode of administration and the magnitude of the desired effect on bone repair.

The drug administered according to the invention can be administered as a single or repeat dose. For repeat-dose administration, it is possible to choose daily continuous administration, 1 to 3 times a day, throughout the duration of the fracture repair (one to several months), or intermittent administration, for example 1 day a week for one to several months.

The dosage unit can comprise from 0.001 mg to 400 mg of bisphosphonic acid derivative(s) of formula (I), more particularly 0.01 mg to 400 mg.

Thus the administration doses of the drug prepared according to the invention can vary from 0.001 mg to 1.2 g per day, more particularly from 0.01 mg to 1.2 g per day.

The dosage unit preferably comprises from 0.1 to 250 mg of bisphosphonic acid derivative(s) of formula (I).

Barbier et al. teach in column 2 lines 25-30, that the preferred bisphosphonates are tiludronic acid and its pharmaceutically acceptable salts.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the compounds of Breliere et al. in the treatment of lameness in horses as Barbier et al. disclose the same compositions suitable for vet nary use (encompassing horses) and the patient population treated by Breliere et al.'s method of treatment for inflammation and arthritis would encompass lameness and thus inherently treat said condition. The examiner respectfully points out the following from MPEP § 2112.01: "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leonard M. Williams whose telephone number is 571-272-0685. The examiner can normally be reached on MF 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER